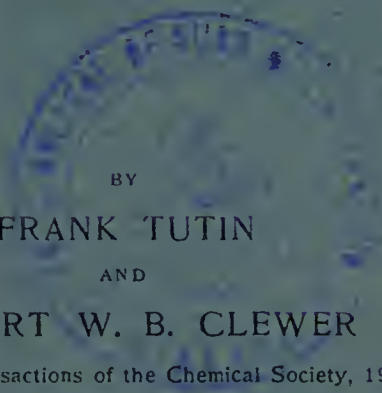
CHEMICAL EXAMINATION

OF

ERIODICTYON

PART II



BY

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XI.—*Chemical Examination of Eriodictyon. Part II.*

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The first part of this investigation of *Eriodictyon* leaves was carried out by one of us in conjunction with Dr. Power, and the results obtained were communicated to the meeting of the American Pharmaceutical Association held at Indianapolis in 1906 (*Proc. Amer. Pharm. Assoc.*, 1906, **54**, 352). In this communication it was shown that the leaves contain, besides essential oil, resins, and other amorphous products, a considerable amount of glucose, the hydrocarbons triacontane and pentatriacontane, formic, acetic, butyric, cerotic, and other acids, both in the free state and as glycerides, and a very small amount of a phytosterol. In addition to these products, three new crystalline substances of a phenolic nature were isolated, namely, eriodictyol, $C_{15}H_{12}O_6$ (m. p. 267°), homoeriodictyol, $C_{16}H_{14}O_6$ (m. p. 223°), and a very small amount of a substance possessing the formula $C_{16}H_{12}O_6$.*

In subsequent communications (Power and Tutin, Trans., 1907, **91**, 887; Proc., 1907, **23**, 243) the results of further work on eriodictyol and homoeriodictyol were described, and the latter substance was shown to possess the following constitution :

A further and larger amount of the extract of *Eriodictyon* leaves has now been worked up in order to obtain the requisite material for the continuation of experiments with eriodictyol and its homologue. During this process a quantity of the product has been accumulated, from which the small amount of the substance, $C_{16}H_{12}O_6$, was isolated. An exhaustive examination of this product has resulted in the isolation of a larger quantity of the last-mentioned compound, the formula and properties of which have been confirmed, together with two other crystalline substances of a phenolic nature, both of which are new compounds.

The substance which was previously isolated in small amount, and which it is now proposed to designate *chrysoeriol*, forms golden-yellow leaflets which do not melt at 337°. It has the formula $C_{16}H_{12}O_6$, and is present in the air-dried leaves to the extent of 0·0093 per cent. of

* In Abstr., 1906, **90**, ii, 885, the formula of this substance is incorrectly given as $C_{15}H_{10}O_6$.

their weight. It contains three hydroxyl groups, since it yields a *triacetyl* derivative, $C_{16}H_{11}O_6(\cdot CO\cdot CH_3)_3$, which melts at 211—212°.

The first of the newly-isolated compounds was obtained in an amount corresponding with 0·0187 per cent. of the weight of the air-dried leaves. It crystallises in yellow needles melting at 258°, and for it the name *xanthoeridol* is proposed. It possesses the formula $C_{18}H_{14}O_7$, and, like chrysoeriol, yields a *triacetyl* derivative (m. p. 175—176°).

The other new compound is represented by the formula $C_{19}H_{18}O_7$, and the amount of it present in the air-dried leaves is equivalent to 0·0117 per cent. of their weight. It forms long, pale yellow, flattened needles, which, after drying in the air, melt at 199°, and contain one molecule of water of crystallisation; the anhydrous substance melts at 209°. There are two substances of the formula $C_{19}H_{18}O_7$ which are stated to melt near 200°, namely, the methyl ester of usnolic acid (Widman, *Annalen*, 1902, **324**, 139), which melts at 202°, and quercetin tetramethyl ether (Kostanecki, Lampe, and Tambor, *Ber.*, 1904, **37**, 1404), which melts at 198°. It was readily ascertained that the compound we have isolated is not identical with methyl usnolate, since it yields a dark purplish-brown colour with ferric chloride, whilst the latter compound gives a green colour. The properties attributed to the tetramethyl ether of quercetin, however, are practically identical with those of the compound we have obtained, and it therefore appeared probable that the two substances might be identical. Through the courtesy of Professor Kostanecki, who supplied us with a specimen of tetramethylquercetin, we were enabled directly to compare the substances in question, when it was found that a mixture of the two preparations melted at about 160°. The substance from eriodictyon leaves is therefore a new compound, and it is proposed to designate it *eriodonol*. When treated with acetic anhydride, eriodonol yields a *tetra-acetyl* derivative (m. p. 131°), thus indicating the presence of four hydroxyl groups.

Experimental.

A quantity of the same alcoholic extract of the leaves of *Eriodictyon Californicum* (Hooker and Arnott), Greene, as had been employed in the first investigation, representing approximately 8580 grams of the air-dried leaves, was mixed with water and steam passed through the mixture for some time. The aqueous liquid was then decanted from the large amount of resin, and the latter again treated several times in a similar manner in order to free it as completely as possible from substances soluble in water. The combined aqueous extracts were then evaporated to a convenient bulk, and repeatedly extracted with

ether. In the former investigation eriodictyol and homoeriodictyol were isolated from this ethereal extract by fractional extraction with a solution of sodium carbonate. It has now been ascertained that these substances are more conveniently obtained, and in better yield, when the ethereal liquid is first extracted with a solution of ammonium carbonate. This latter treatment removes from the ethereal solution a large amount of sticky, uncrystallisable matter of an acidic nature, from which nothing definite could be isolated. Extraction of the ethereal liquid with sodium carbonate solution then yields a precipitate of the monosodium compound of homoeriodictyol, and the filtrate from the latter, on acidification, gives a product consisting very largely of eriodictyol. This product has been exhaustively examined, but was found to contain no crystalline substance other than eriodictyol.

The large amount of resin referred to above, which had been freed from substances soluble in water, was mixed with purified sawdust and successively extracted in a Soxhlet apparatus with petroleum (b. p. 33—50°) and ether, but only the extract obtained by the latter solvent was examined in the present investigation. It was from this ethereal extract that the greater part of the homoeriodictyol was obtained, and here again the isolation of this substance is greatly facilitated by first removing from the ethereal liquid the substances soluble in a solution of ammonium carbonate.

On shaking the ethereal extract of the resins with a solution of ammonium carbonate, a very large quantity of the ammonium salt of an acidic resin separates in the form of a heavy, dark green tar, on the surface of which is a brown, aqueous layer. Nothing crystalline could be obtained from either of these products, the former yielding upwards of a kilogram of a nearly hard, green resin. The ethereal liquid, after considerable dilution, was then exhaustively extracted by shaking with successive portions of a solution of sodium carbonate. The large amount of the crystalline sodium compound of homoeriodictyol suspended in the alkaline liquids thus obtained was rapidly collected and washed, first with ether, and subsequently with a little water. The aqueous portion of the filtrate was then immediately acidified, as it rapidly absorbs oxygen on exposure to the air. The sodium compound was recrystallised from water, after which the mother liquors were acidified, and the precipitated product added to the material obtained on acidifying the original filtrate from the sodium derivative. The total amount of this material from the mother liquors was dissolved in ether, freed from some tarry decomposition products by means of ammonium carbonate solution, and then extracted by shaking with successive portions of a solution of sodium carbonate, when a number of fractions were obtained. Most of these fractions contained some of the sodium compound of homoeriodictyol,

which was removed by filtration. The filtrate from the first fraction was discarded, for it was dark green, and, on acidification, yielded only resinous matter, but all the subsequent alkaline, aqueous liquids possessed a clear dark orange colour. They were therefore mixed, acidified, and extracted with ether.

The ethereal solution thus obtained would contain the whole of the high-melting, yellow, phenolic substance, which was previously isolated in small amount by Power and Tutin (*loc. cit.*), and it also gave evidence of containing some eriodictyol. Moreover, in the original investigation by the above-mentioned authors, indications were obtained of the presence of a third compound, crystallising in yellow needles which melted at about 255°. In order, therefore, to render possible the isolation of the constituents of this mixture, advantage was taken of the fact that, in all probability, the several components would vary in their respective affinities for alkali. The material dissolved in the ether was therefore systematically extracted, in fractions, by thoroughly shaking the ethereal solution with thirty-four successive portions of a 5 per cent. solution of sodium carbonate. For each of the first fifteen extractions, 20 c.c. of the solution were employed, and for each of the next ten extractions, 50 c.c., the remaining extractions being accomplished with 100 c.c. each. In every case the alkaline solution was acidified immedately after separation from the ether.

The first and last fractions obtained yielded only resinous matter, but the remainder all contained crystalline products, although each of them also contained some resin. Fractions 2 to 13 inclusive yielded a substance, designated *xanthoeridol*, which formed yellow needles, melting at 258°. Eriodictyol was obtained from fractions 4 to 26 inclusive, and this compound was by far the largest constituent of the mixture. *Chrysoeriol*, the yellow substance previously obtained in small amount by Power and Tutin, occurred in fractions 15 to 26 inclusive, whilst fractions 27 to 33 inclusive yielded a fourth compound, *eriodonol*, which melts at 209°.

Xanthoeridol, $C_{18}H_{11}O_4(OH)_3$.

Fractions 2 to 13 inclusive, above referred to, yielded a product (1·6 grams) which crystallised from a mixture of ethyl acetate and alcohol in tufts of soft, yellow needles melting at 258°:

0·1146 gave 0·2643 CO_2 and 0·0441 H_2O. C = 62·9; H = 4·3.

$C_{18}H_{14}O_7$ requires C = 63·1; H = 4·1 per cent.

The properties of this substance do not agree with those of any compound of the formula $C_{18}H_{14}O_7$ which has previously been described. It is proposed, therefore, to designate it *xanthoeridol*.

Xanthoeridol dissolves in alkalis and in concentrated sulphuric acid.

giving a bright yellow colour, and its solution in dilute alcohol is rendered dark brown by ferric chloride.

Triacetylxanthoeridol, $C_{18}H_{11}O_7(CO\cdot CH_3)_3$.—A small quantity of xanthoeridol was boiled for thirty minutes with an excess of acetic anhydride, the greater part of the latter was then removed, and the residue diluted with ether. *Triacetylxanthoeridol* then separates in tufts of slightly yellow needles, which melt at about 169°. After recrystallisation from acetic anhydride, the melting point was raised to 175—176°:

0·1082 gave 0·2443 CO_2 and 0·0441 H_2O. C = 61·6; H = 4·5.
$C_{24}H_{20}O_{10}$ requires C = 61·5; H = 4·3 per cent.

Chrysoeriol, $C_{16}H_9O_3(OH)_3$.

In the first part of this work (*loc. cit.*, p. 367) Power and Tutin described the isolation of a small amount (0·3 gram) of a new, yellow, crystalline substance of phenolic nature, possessing the formula $C_{16}H_{12}O_6$. As so small an amount of this compound was obtained, no name was then given to it. The present authors, however, having now obtained it in larger amount (0·8 gram), and fully confirmed the formula and properties previously assigned to it, propose to designate it *chrysoeriol*.

Chrysoeriol is very sparingly soluble in alcohol, and hence was easily separated from the eriodictyol with which it was associated. On allowing its solution in boiling alcohol to evaporate, it separates in feathery leaflets possessing a golden-yellow colour. It does not melt when heated to 337°:

0·0873 gave 0·2050 CO_2 and 0·0328 H_2O. C = 64·0; H = 4·2.
$C_{16}H_{12}O_6$ requires C = 64·0; H = 4·0 per cent.

Chrysoeriol yields colour reactions which are similar to those of xanthoeridol.

Triacetylchrysoeriol, $C_{16}H_9O_6(CO\cdot CH_3)_3$.—A small quantity of chrysoeriol was boiled for thirty minutes with an excess of acetic anhydride. The anhydride was then decomposed with water, and the resulting solid collected. On crystallisation from a mixture of ethyl acetate and alcohol, the *acetyl* derivative separated in tufts of almost colourless needles, which melted at 200°. After one recrystallisation from ordinary alcohol, the melting point was 196—199°, and, after being boiled for two hours with dilute alcohol, the substance melted indefinitely from 168—178°. This behaviour is evidently due to the fact that triacetylchrysoeriol readily undergoes partial hydrolysis when heated with solvents containing water. When crystallised from acetic anhydride, it melted at 211—212°:

0·0987 gave 0·2244 CO_2 and 0·0393 H_2O. C = 62·0; H = 4·4.
$C_{22}H_{18}O_9$ requires C = 62·0; H = 4·2 per cent.

Eriodonol, $C_{19}H_{14}O_3(OH)_4$.

The last fractions of material obtained by the above-described fractional extraction with sodium carbonate solution contained a considerable proportion of green, resinous matter, together with a substance which slowly crystallised from slightly diluted alcohol in long, flattened needles, possessing a pale yellow colour. After drying in the air, this compound melted at about 199°, but, after drying at 110° for a short time, fusion occurred at 209°. The total amount obtained was 1 gram:

0·3779, on drying at 110°, lost 0·0174 H_2O. H_2O = 4·6.
0·1245 of anhydrous substance gave 0·2907 CO_2 and 0·0561 H_2O.
C = 63·7; H = 5·0.
$C_{19}H_{18}O_7,H_2O$ requires H_2O = 4·8 per cent.
$C_{19}H_{18}O_7$ requires C = 63·7; H = 5·0 per cent.

In order further to confirm the formula of this compound, a molecular-weight determination was made:

0·2400 in 30 of acetic acid gave Δ^t – 0·090°. M.W. = 351.
$C_{19}H_{18}O_7$ requires M.W. = 358.

This compound, as previously stated (p. 82), is not identical with any substance hitherto described, and the name *eriodonol* is suggested for it. Eriodonol is very readily soluble in ethyl acetate, and dissolves readily in absolute ethyl and methyl alcohols, separating from the last-named solvents in tufts of small needles which are practically anhydrous.

When treated with concentrated sulphuric acid, crystals of eriodonol first become orange-coloured, and then dissolve, giving a yellow solution which exhibits a slight fluorescence. Eriodonol yields with ferric chloride a dark purplish-brown colour, and dissolves in alkalis, giving a not very readily soluble sodium derivative, the solution of which is bright yellow. The tinctorial properties of eriodonol are similar to those of the tetramethyl ether of quercetin described by Kostanecki, Lampe, and Tambor (*loc. cit.*), namely, it dyes linen mordanted with alumina or iron, bright yellow or dark brown respectively. Eriodonol yields iodoform when warmed with iodine and sodium carbonate solution, differing in this respect from xanthoeridol and chrysoeriol.

Tetra-acetyleriodonol, $C_{19}H_{14}O_7(CO\cdot CH_3)_4$.—A small amount of eriodonol was acetylated by boiling with an excess of acetic anhydride, but the resulting *acetyl* derivative crystallised only with difficulty. It was practically insoluble in cold alcohol, being deposited as an oil

on allowing its solution in this solvent to cool. It is most conveniently crystallised by concentrating its solution in acetic anhydride to a small bulk, diluting this with ether, and then adding light petroleum On allowing the mixture to stand for a few days, the acetyl derivative separates in tufts of colourless needles, which melt at 131°:

0·1052 gave 0·2370 CO_2 and 0·0451 H_2O. C = 61·5; H = 4·8.

$C_{27}H_{26}O_{11}$ requires C = 61·6; H = 4·9 per cent.

It is thus apparent that eriodonol contains four hydroxyl groups, but, as its acidic properties are so slight, it is probable that not more than one of them is phenolic.

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